Serial No. 10/014,363 Filed: December 11, 2001

In the Specification:

Please amend the specification as follows:

Please delete paragraphs [0013-0017] and replace them with the following amended paragraphs:

Figure 1: Shows the primary structure of human EPO (165 amino acids) (SEQ ID NO: 1).

Figure 2: Shows the primary structure of human EPO (166 amino acids) (SEQ ID NO: 2).

Figure 3: Shows the primary structure and corresponding nucleic acid sequence (SEQ ID NO: 6) of the APPRIEGR-EPO (SEQ ID NO: 3). The underlined amino acid sequence corresponds to the secretion signal sequence, the wavy line to the amino acid sequence specific for the proteolytic cleavage site.

Figure 4: Shows the primary structure and corresponding nucleic acid sequence (SEQ ID NO: 7) of APP-EPO (SEQ ID NO: 4). The underlined amino acid sequence corresponds to the secretion signal sequence, the wavy line to the amino acid sequence specific for the proteolytic cleavage site.

Figure 5: Shows the primary structure and corresponding nucleic acid sequence (SEQ ID NO: 8) of APPGAAHY-EPO (SEQ ID NO: 5). The underlined amino acid sequence corresponds to the secretion signal sequence, the wavy line to the amino acid sequence specific for the proteolytic cleavage site.

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Please delete paragraph [0054] and replace it with the following amended paragraph:

Suitable proteases for cleavage of fusion proteins are described by Carter, P: Site-specific proteolysis of fusion proteins; Protein Purification: From Molecular Mechanisms to Large Scale Processes, ACS, Washington DC, pp. 181 - 193 (1990). Such proteases require a narrow specificity to cleave selectively at their recognition sequence and not anywhere in the target protein sequence. Examples are factor Xa which cleaves at IEGR↓ (SEQ ID NO: 9) and enterokinase which cleaves at DDDDK↓ (SEQ ID NO: 10). Moreover enterokinase is reported to cleave DDDDK↓AP (SEQ ID NO: 11) which indicates specificity at the P1' and P2' site for interleukins (P. Carter). Enterokinase is, however, not preferred if chemical protecting agents to protect the side chain ε-amino groups of lysines have to be introduced. In such case, the enzyme would no longer work at the wanted cleaving site.

Please delete paragraph [0077] and replace it with the following amended paragraph:

A further embodiment of the invention relates to erythropoietin glycoproteins comprising the amino acid sequences as shown in Fig. 1 and Fig. 2 having a N-terminal peptidic extension which represents a proteolytic cleavage site, optionally comprising an N-terminal purification tag. Examples for these peptides are APPRIEGR-EPO (SEQ ID NO: 3), APP-EPO (SEQ ID NO: 5) (see also Figs. 3 to 5).

Please delete paragraph [0082] and replace it with the following amended paragraph:

The wild type erythropoietin coding fragment was obtained by methods known in the art, e.g. as described by Jacobs K. et al., Nature 313, 806-10 (1985). Preferably, the coding fragment

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is amplified using primers EPO-EcoRI 5'-GAGCCTGAATTCACCACC (SEQ ID NO: 12) and EPO-SalI 5'-AGGTGGGTCGACCTGGTCAT CTGTCCCCTG (SEQ ID NO: 13). The PCR fragment was digested with EcoRI and SalI (sites are underlined in primer sequences) and cloned into the multiple cloning site of the pre-digested pCI-dhfr vector fragment. Expression of the EPO gene was therefore under control of the human cytomegalovirus (CMV) immediate-early enhancer/promoter region, an optimized chimeric intron for regulated expression and the SV40 late polyadenylation signal.

Please delete paragraph [0083] and replace it with the following amended paragraph:

Please delete paragraph [0085] and replace it with the following amended paragraph: